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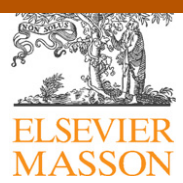

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CLINICAL RESEARCH

Regional system of care for ST-segment elevation myocardial infarction in the Northern Alps: A controlled pre- and postintervention study

Réseau de prise en charge de l'infarctus du myocarde avec sus-décalage du segment ST dans les Alpes du Nord : étude avant-après contrôlée

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KEYWORDS
Cohort studies;
Emergency medical services;

Summary
Background. — Regionalization of care for ST-segment elevation myocardial infarction (STEMI) has been advocated, although its effect on processes of care and clinical outcomes remains uncertain.

Abbreviations: FAST-MI, French registry of Acute ST-elevation and non-ST-elevation Myocardial Infarction; IQR, interquartile range; PCI, percutaneous coronary intervention; RESURCOR, RESeau d'URgences CORonariennes; STEMI, ST-segment elevation myocardial infarction.

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Myocardial infarction;
Outcome and process assessment;
Regional medical programmes

Aim. — To assess the impact of a regional system of care on provision of reperfusion therapy for STEMI patients relative to control hospitals.
Methods. — We analysed the original data from two nationwide prospective cohort studies conducted in 2000 and 2005, respectively. Overall, 160 hospitals participated in both studies, including seven hospitals involved in a regional system of care implemented in the Northern Alps in 2002 and 153 control hospitals located in other French areas.
Results. — A total of 102 and 2377 STEMI patients were enrolled in Northern Alps and control hospitals, respectively. Overall, patients enrolled in 2005 were more likely to receive any reperfusion therapy (60% vs 52%; $P < 0.001$), prehospital fibrinolysis (33% vs 15%; $P < 0.001$), and primary percutaneous coronary intervention (32% vs 26%; $P < 0.001$) than those enrolled in 2000. However, the regional system of care was associated with a larger absolute change in the use of prehospital fibrinolysis (45.0 vs 17.0; $P = 0.02$) and rescue or early routine coronary angiography or intervention after fibrinolysis (35.3 vs 15.2; $P = 0.01$). Patients enrolled in 2005 had lower adjusted hazard ratios for death (0.70, 95% confidence interval 0.57—0.87; $P = 0.001$), with no significant interaction between study groups.
Conclusion. — Regionalization of care for STEMI patients improves access to reperfusion therapy, although its impact on clinical outcomes deserves further study.

MOTS CLÉS
Études de cohorte ;
Évaluation des processus et des résultats ;
Infarctus du myocarde ;
Réseaux de soins ;
Services d'urgence

Résumé
Contexte. — Les recommandations préconisent une coordination régionale de la prise en charge de l'infarctus du myocarde avec sus-décalage du segment ST (STEMI).
Objectif. — Évaluer l'impact d'un réseau de soins dédié à la prise en charge des patients avec un STEMI.
Méthodes. — Nous avons analysé les données originales provenant de deux études de cohorte prospectives multicentriques conduites en France en 2000 et 2005. Au total, 160 hôpitaux ont participé aux deux études, dont sept hôpitaux impliqués dans un réseau de soins mis en place en 2002 dans les Alpes du Nord et 153 hôpitaux témoins situés sur le reste du territoire national.
Résultats. — Cent deux patients ont été inclus dans les hôpitaux des Alpes du Nord et 2377 dans les hôpitaux situés sur le reste du territoire national. Globalement, les patients recrutés en 2005 avaient plus souvent eu accès à une fibrinolyse préhospitalière (33 % versus 15 % ; $p < 0{,}001$) ou à une angioplastie coronaire percutanée primaire (32 % versus 26 % ; $p < 0{,}001$). Cependant, le réseau de soins était associé à une augmentation plus importante de la proportion de patients avec une fibrinolyse préhospitalière (45 % versus 17 % ; $p = 0{,}02$) et une angioplastie coronaire percutanée secondaire ou de sauvetage (35 % versus 15 % ; $p = 0{,}01$). Le risque de décès était plus faible en 2005 (0,70, intervalle de confiance à 95 % 0,57—0,87 ; $p = 0{,}001$), sans qu'on puisse mettre en évidence de différence en fonction du groupe.
Conclusion. — La mise en place d'un réseau de soins a amélioré l'accès aux stratégies de revascularisation des patients admis avec un STEMI dans les hôpitaux des Alpes du Nord.

Background

Prompt coronary reperfusion therapy for ST-segment elevation myocardial infarction (STEMI) limits infarct size and improves survival [1]. Current guidelines advocate primary percutaneous coronary intervention (PCI) as the preferred method for reperfusion in STEMI as long as the expected time from the first medical contact to the coronary balloon inflation is less than 2 hours [2,3]. Otherwise, patients should receive fibrinolysis therapy, preferably administered prehospital [4], and then be directed to a PCI-capable centre where coronary angiography and intervention can be performed in a time window of 3—24 hours [5].

Unfortunately, STEMI registries consistently report delays in reperfusion that exceed those recommended by guidelines and substantial proportions of patients who are denied any reperfusion therapy [1,6—8]. Because the reasons for these observations are partly related to systemic barriers [9,10], systems of care have been developed through regional networks to broaden the use of reperfusion therapy and to facilitate timely access to primary PCI for patients presenting to hospitals without PCI capability [11,12].

Several studies have reported a significant reduction in time to reperfusion therapy and increased access to primary PCI following the implementation of regional systems of care for STEMI [13—18]. However, these studies did not include regional or national comparators [15,17,18], lacked a historical control group [13,14] or had limited generalizability because of their location in large urban areas [16].

Pooling the original data from two prospective cohort studies, we examined the impact of a regional system of care on the provision of reperfusion therapy for STEMI patients relative to a nationwide sample of control hospitals.

Methods

Study design

We retrospectively designed a controlled pre- and postintervention study evaluating a regional system of care that was implemented in October 2002 in the Northern Alps in France. Pre- and postintervention data were extracted from the USIC 2000 and French registry of Acute ST-elevation and non-ST-elevation Myocardial Infarction (FAST-MI) studies, which were conducted in 2000 and 2005, respectively. To adjust for secular trends and sudden changes [19], hospitals located in other French mainland areas served as controls.

The rationale, design and primary outcomes of the USIC 2000 and FAST-MI studies have been described in detail elsewhere [20,21]. Briefly, the two studies were nationwide prospective observational cohort studies designed to collect complete and representative data on processes of care and clinical outcomes for patients with acute myocardial infarction who were admitted to participating hospitals over a 1-month period in France.

Study sites

The USIC 2000 and FAST-MI studies involved 316 and 222 hospitals with intensive care units, respectively. Of these, 160 hospitals participated in both studies, including seven Northern Alps hospitals involved in the regional system of care and 153 control hospitals (Table 1).

Patients

Physicians at participating hospitals enrolled consecutive patients 24 hours/day, 7 days/week, over a 1-month period (i.e. in November 2000 for the USIC 2000 study and in October 2005 for the FAST-MI study). Adult patients were eligible if they had: concentrations of serum markers of myocardial necrosis (creatine kinase, creatine kinase-MB, troponin I or troponin T) that were more than twice the upper limit of the normal range; and either symptoms consistent with acute myocardial infarction or electrocardiographic changes in at least two contiguous leads (Q waves $\geq$ 0.04 seconds in duration, persistent ST-segment elevation or depression $\geq$ 0.1 mV). The time from symptom onset to intensive care unit admission had to be less than 48 hours.

For the present analysis, we focused on patients with ST-segment elevation or a presumed new Q wave or left bundle-branch block on the first electrocardiogram recorded. The number of patients enrolled in the two original studies determined the sample size and no formal calculation of sample size was performed for this post hoc analysis.

Data collection

Using a case report form, attending physicians or clinical research technicians collected detailed information on demographics, cardiovascular history, risk factors, comorbid conditions, treatments prior to admission, presenting characteristics, cardiac procedures, medications used within 48 hours of admission and discharge medications. We also

Table 1 Site of admission characteristics in 2005.

Characteristics	Northern Alps hospitals (n = 7)	Control hospitals (n = 153)
Ownership		
Public	6 (85.7)	112 (73.2)
Private, for-profit	1 (14.3)	32 (20.9)
Private, not-for-profit	— (—)	7 (4.6)
Veterans Affairs	— (—)	2 (1.3)
Academic hospitals	1 (14.3)	27 (17.6)
Region		
Paris and surrounding area	— (—)	26 (17.0)
Northwest	— (—)	26 (17.0)
Northeast	— (—)	49 (32.0)
Southeast	7 (100)	26 (17.0)
Southwest	— (—)	26 (17.0)
Licensed beds		
< 200	1 (14.3)	42 (27.5)
200—599	4 (57.1)	81 (52.9)
$\geq$ 600	2 (28.6)	30 (19.6)
Cardiac procedure capabilities[a]		
Cardiac catheterization	4 (57.1)	94 (61.4)
PCI	3 (42.9)	90 (58.8)
CABG	2 (28.6)	39 (25.5)

Data are n (%). CABG: coronary artery bypass graft; PCI: percutaneous coronary intervention.
[a] In 2000, four Northern Alps and 92 control hospitals had cardiac catheterization capabilities, two Northern Alps and 82 control hospitals had percutaneous coronary capabilities and two Northern Alps and 35 control hospitals had coronary artery bypass graft capabilities.

documented the characteristics of the admitting hospital (i.e. location in the Northern Alps, academic status, ownership, region, number of licensed beds and cardiac procedure capabilities). Hospitals were identified as academic hospitals based on whether or not they were affiliated with a university [22]. Consistent with a previous study [23], we defined PCI centres as hospitals that offered emergency PCI 24 hours/day, 7 days/week.

Regional system of care

The RESeau d'URgences CORonariennes (RESURCOR) is a coordinated regional system of care for STEMI, which was implemented in the Northern Alps in October 2002. It involves all 15 acute care hospitals (including three PCI centres), three emergency medical system call centres and 12 mobile emergency care units, regardless of their affiliation. The Northern Alps is a predominantly mountainous area covering 15,000 km^2, with an estimated population of 1,860,000 inhabitants and large seasonal variations due to tourism. The median distance and driving time from each community hospital to the closest PCI centre were 63 km (range 4.5—132 km) and 43 minutes (range 10—88 minutes), respectively. The rationale and primary outcomes of the RESURCOR have been reported in detail elsewhere [24].

As part of the RESURCOR, a triage algorithm and a set of treatment protocols for coronary reperfusion were established according to published guidelines and available resources, and were approved by representatives of the emergency medical system call centre, mobile emergency care unit, emergency department, coronary care unit and interventional staff. The triage algorithm and treatment protocols were disseminated through pocket cards (Fig. 1) and booklets, and were made available on a dedicated website (www.renau.org). The recommendations were reviewed and eventually updated according to the most recent published evidence on a yearly basis.

Briefly, the triage algorithm recommended that physicians at emergency medical system call centres who received a call from a patient with symptoms suggestive of acute myocardial infarction lasting less than 12 hours dispatch a mobile emergency care unit [25]. Mobile emergency care units were staffed by emergency or critical care physicians who might administer prehospital fibrinolysis or

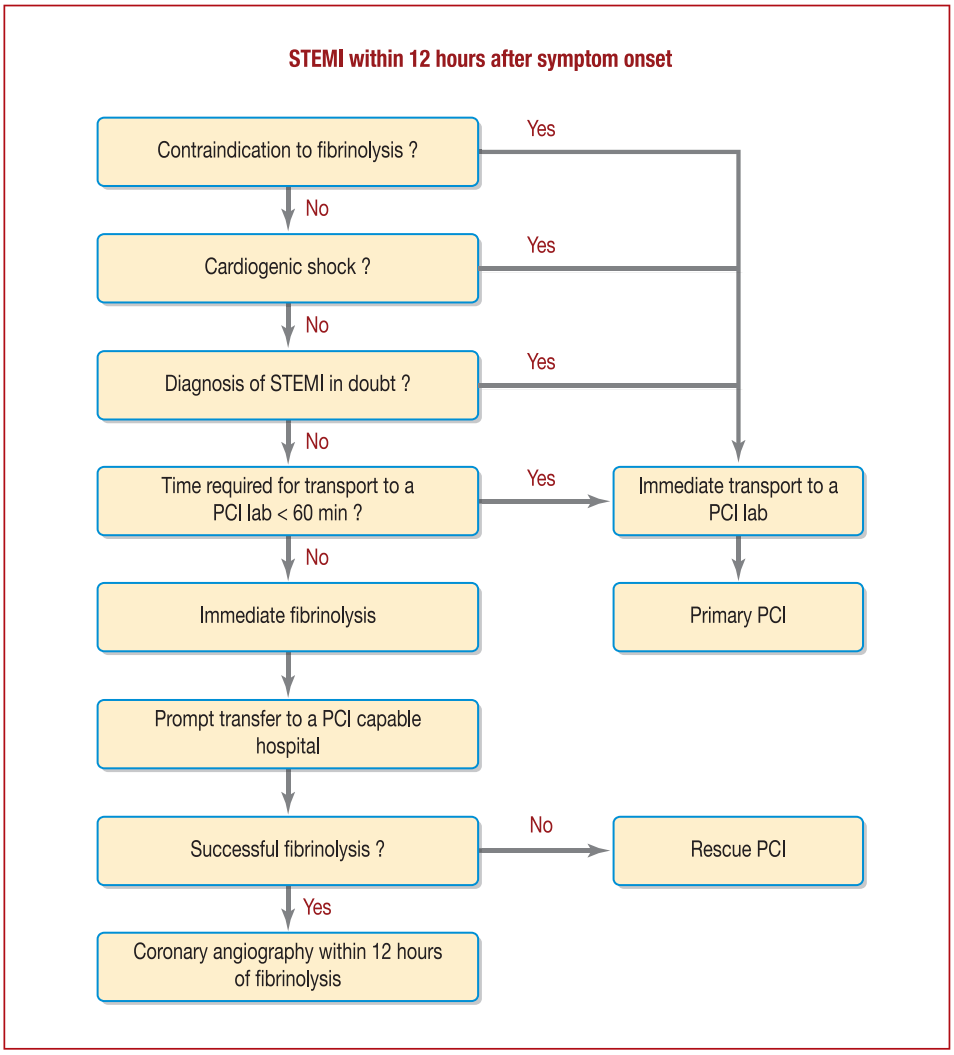

Figure 1. Options for initial reperfusion therapy for patients presenting with ST-segment elevation myocardial infarction (STEMI) (2002). PCI: percutaneous coronary intervention.

activate the closest catheterization laboratory en route for primary PCI, depending on anticipated delays in reperfusion. Emergency department physicians at hospitals without PCI capability evaluated self-transported STEMI patients with symptoms lasting less than 12 hours for reperfusion with either primary PCI at the closest PCI centre or hospital fibrinolysis. Our triage protocol advocated that patients undergo rescue PCI after failed fibrinolysis and routine early coronary angiography and intervention within 12 hours of successful fibrinolysis [26]. Patients transferred for primary PCI were transported by mobile emergency care units and taken directly to the catheterization laboratory without re-evaluation in the emergency department.

An ongoing registry collected prospective detailed data on time to treatment, clinical baseline characteristics and coronary angiography findings, to provide each hospital with feedback on aggregated quality data. Physicians were invited to an annual meeting where the overall policy of the RESURCOR and the trends in timely reperfusion therapy were presented and discussed [27].

Outcome measures

The primary effectiveness outcome was the receipt of any reperfusion therapy, either with primary PCI or fibrinolysis. The secondary effectiveness outcomes included the receipt of prehospital fibrinolysis, any (i.e. either prehospital or hospital) fibrinolysis, primary PCI and rescue or routine early coronary angiography or intervention after fibrinolysis.

The clinical outcome was 1-year all-cause mortality. Death was determined from medical records and follow-up telephone interviews with the patients' relatives or their primary care physician 1 year after the index admission. The living status of patients lost to follow-up was ascertained using their birthplace census record.

Statistical analysis

Categorical variables were expressed as frequency and percentage and continuous variables as median and 25th and 75th percentiles (interquartile range [IQR]). Differences in baseline characteristics and acute medications between pre- and postintervention periods within each study group were compared using the Wilcoxon rank sum test for continuous variables and the chi-square test or Fisher's exact test when appropriate for categorical variables.

To account for the study design, we compared the primary and secondary effectiveness outcomes using a logistic regression model that contained the study group (i.e. Northern Alps versus control hospitals), study period (pre- versus postintervention period) and a first-order interaction between study group and period. We computed absolute change between 2000 and 2005 within each study group, then we derived differences in change between study groups from the logistic regression models [28]. We computed *P* values and 95% confidence intervals based on the standard errors estimated by the delta method.

We used Kaplan—Meier estimates and the stratified log-rank test to compare the cumulative 1-year mortality across study groups between 2000 and 2005. In multivariable analysis, we estimated hazard ratios for death using a Cox proportional hazard model after adjusting for age, gender, systolic blood pressure and previous myocardial infarction.

Two-sided *P* values less than 0.05 were considered statistically significant. All analyses were performed using Stata version 11.0 (Stata Corporation, College Station, TX, USA).

Results

The analytical sample comprised 2479 STEMI patients, including 102 patients admitted to seven Northern Alps hospitals and 2377 patients admitted to 153 control hospitals. More patients were enrolled in 2005 than in 2000 in both study groups (34 and 1076 in 2000 vs 68 and 1301 in 2005, respectively).

The median age for all patients was 66 years (IQR, 53—77 years), 1762 (71%) were men, 512 (21%) presented with a Killip class II or higher and 1373 (55%) were admitted by a mobile emergency care unit. In 2005, a higher percentage of patients were admitted to PCI centres and had a medical history of hypertension in both study groups (Table 2). Enrolment in 2005 was also associated with higher blood pressure on admission, higher prevalence of family history of coronary artery disease and more frequent use of statins for control hospitals only, although our study was likely to be underpowered to detect differences of similar magnitude for the Northern Alps study group. In contrast, patients admitted to control hospitals in 2005 were less likely to report delayed presentation or a medical history of previous myocardial infarction or peripheral vascular disease.

Overall, patients enrolled in 2005 were more likely to receive any reperfusion therapy (60% vs 52%; $P < 0.001$), prehospital fibrinolysis (33% vs 15%; $P < 0.001$) and primary PCI (32% vs 26%; $P < 0.001$) than those enrolled in 2000. The absolute change in the use of prehospital fibrinolysis was greater for Northern Alps hospitals (Table 3), with a parallel increase in the percentage of patients undergoing rescue or early routine coronary angiography or intervention after fibrinolysis (Table 3).

Between 2000 and 2005, the median time from symptom onset to fibrinolysis decreased from 180 minutes (IQR 120—240 minutes) to 130 minutes (IQR 90—210 minutes), while the median time from symptom onset to primary PCI increased from 240 minutes (IQR 150—360 minutes) to 293 minutes (IQR 195—510 minutes) and the median time from admission to primary PCI increased from 45 minutes (IQR 20—80 minutes) to 60 minutes (IQR 25—144 minutes) ($P < 0.001$ for all comparisons). Enrolment in 2005 was associated with a more frequent use of low-molecular-weight heparin, platelet glycoprotein IIb/IIIa receptor agonists and statins for Northern Alps and control hospitals (Table 4).

Patients enrolled in 2005 experienced lower 1-year mortality rates than those enrolled in 2000 in the Northern Alps (7.4% vs 8.8%) and control (12.6% vs 16.8%) hospitals ($P = 0.002$) (Fig. 2). In multivariable analysis, enrolment in 2005 remained associated with a decreased adjusted hazard ratio for death (0.70, 95% confidence interval 0.57—0.87; $P = 0.001$), with no significant interaction between study groups (adjusted hazard ratios 0.77 and 0.70 for Northern

Table 2 Baseline characteristics stratified by study year for patients enrolled in Northern Alps and control hospitals.

Characteristics[a]	Northern Alps hospitals			Control hospitals		
	2000 ($n=34$)	2005 ($n=68$)	P	2000 ($n=1076$)	2005 ($n=1301$)	P
Male sex	27 (79.4)	51 (75.0)	0.62	776 (72.1)	908 (69.8)	0.21
Age (years)	67 (55—78)	65 (54—77)	0.74	67 (53—76)	66 (53—77)	0.91
Admission by mobile emergency care unit	22 (64.7)	38 (55.9)	0.39	611 (56.8)	702 (54.0)	0.17
Admission to hospital with PCI capability	19 (55.9)	58 (85.3)	0.001	768 (71.4)	1040 (79.9)	< 0.001
Presentation within 3 hours of symptom onset	11 (32.3)	25 (36.8)	0.66	284 (27.6)	571 (43.9)	< 0.001
Presenting characteristics						
Heart rate (beats/minute)	80 (67—88)	74 (60—90)	0.79	75 (65—90)	77 (65—90)	0.30
Systolic blood pressure (mmHg)	122 (110—140)	130 (115—148)	0.38	130 (114—150)	133 (116—150)	0.006
Killip class			0.14			0.20
I	29 (85.3)	57 (83.8)		850 (79.1)	1028 (79.1)	
II	1 (2.9)	8 (11.8)		143 (13.3)	155 (11.9)	
III	2 (5.9)	3 (4.4)		52 (4.8)	86 (6.6)	
IV	2 (5.9)	0 (0)		30 (2.8)	30 (2.3)	
LVEF $\leq$ 35%	2 (6.5)	7 (11.7)	0.71	136 (14.0)	146 (14.0)	0.98
Anterior ST-segment elevation	11 (32.4)	22 (32.4)	0.99	413 (38.4)	496 (38.1)	0.90
Medical history						
Diabetes mellitus	6 (17.7)	9 (13.2)	0.56	227 (21.1)	264 (20.3)	0.63
Hypertension	9 (26.5)	33 (48.5)	0.03	485 (45.1)	661 (50.8)	0.005
Hypercholesterolaemia	10 (29.4)	25 (36.8)	0.46	437 (40.6)	564 (43.4)	0.18
Current smoking	11 (32.4)	24 (35.3)	0.77	383 (35.6)	463 (35.6)	0.99
Family history of CAD	7 (20.6)	20 (29.4)	0.34	174 (16.2)	314 (24.1)	< 0.001
Peripheral arterial disease	3 (8.8)	4 (6.1)	0.69	98 (9.1)	88 (6.8)	0.04
Previous stroke	1 (2.9)	0 (0)	0.34	45 (4.2)	62 (4.8)	0.49
Previous myocardial infarction	3 (8.8)	8 (11.8)	0.75	176 (16.4)	164 (12.6)	0.009
Previous PCI	1 (2.9)	4 (5.9)	0.66	89 (8.3)	123 (9.5)	0.31
Previous CABG	1 (2.9)	1 (1.5)	0.99	35 (3.3)	38 (2.9)	0.64
Previous congestive heart failure	2 (5.9)	1 (1.5)	0.27	53 (4.9)	58 (4.5)	0.60
Chronic renal disease	2 (5.9)	2 (3.0)	0.60	43 (4.0)	54 (4.2)	0.84
Previous use of medical therapy						
Antiplatelet agents	3 (8.8)	11 (16.2)	0.38	252 (23.4)	298 (22.9)	0.77
Beta-blockers	2 (5.9)	9 (13.2)	0.33	201 (18.7)	242 (18.6)	0.96
Statins	3 (8.8)	12 (17.6)	0.37	189 (17.6)	293 (22.5)	0.003
ACE inhibitors	5 (14.7)	9 (13.2)	0.84	153 (14.2)	192 (14.8)	0.71

Data are number (%) or median (25th—75th percentiles). ACE: angiotensin-converting enzyme; CABG: coronary artery bypass graft; CAD: coronary artery disease; LVEF: left ventricular ejection fraction; PCI: percutaneous coronary intervention.

[a] Values were missing for age ($n=1$), time to presentation ($n=51$), heart rate ($n=17$), systolic blood pressure ($n=19$), Killip class ($n=3$), left ventricular ejection fraction ($n=374$), peripheral arterial disease ($n=5$), previous stroke ($n=4$), previous congestive heart failure ($n=4$) and chronic renal disease ($n=5$).

Table 3 Reperfusion therapy stratified by study year for patients enrolled in Northern Alps and control hospitals.

Revascularization strategy	Northern Alps hospitals			Control hospitals			Percentage point difference in change (95% CI)	*P*
	2000	2005	Absolute change (%)	2000	2005	Absolute change (%)		
Any reperfusion	17/34 (50.0)	42/68 (61.8)	11.8	557/1076 (51.8)	778/1301 (59.8)	8.0*	3.8 (−17.1 to 24.5)	0.72
Fibrinolysis	11/34 (32.3)	33/68 (48.5)	16.2	278/1076 (25.8)	345/1301 (26.5)	0.7	15.5 (−4.5 to 35.5)	0.13
Prehospital fibrinolysis[a]	4/22 (18.2)	24/38 (63.2)	45.0*	89/611 (14.6)	222/702 (31.6)	17.0*	28.0 (5.2 to 50.6)	0.02
Primary PCI	6/34 (17.6)	9/68 (13.2)	−4.4	279/1076 (25.9)	433/1301 (33.3)	7.3*	−11.7 (−27.3 to 3.8)	0.14
Rescue or routine PCI	3/34 (8.8)	30/68 (44.1)	35.3*	74/1076 (6.9)	288/1301 (22.1)	15.2*	20.1 (4.6 to 35.4)	0.01

Data are *n*/*n* (%) unless otherwise indicated. CI: confidence interval; PCI: percutaneous coronary intervention.
[a] The percentage of patients receiving prehospital fibrinolysis was computed among patients admitted by mobile emergency care units.
* $P < 0.01$.

Table 4 Acute medications and length of stay stratified by study year for patients enrolled in Northern Alps and control hospitals.

	Northern Alps hospitals			Control hospitals		
	2000 (*n* = 34)	2005 (*n* = 68)	*P*	2000 (*n* = 1076)	2005 (*n* = 1301)	*P*
Acute medications						
Unfractionated heparin	31 (91.2)	41 (60.3)	0.001	854 (79.4)	861 (66.2)	< 0.001
Low-molecular-weight heparin	1 (2.9)	53 (77.9)	< 0.001	313 (29.1)	800 (61.5)	< 0.001
Platelet glycoprotein IIb/IIIa receptor agonists	4 (11.8)	24 (35.3)	0.02	235 (21.8)	458 (35.2)	< 0.001
Antiplatelet agents	31 (91.2)	65 (95.6)	0.40	1033 (96.0)	1247 (95.8)	0.85
Beta-blockers	19 (55.9)	53 (77.9)	0.02	779 (72.4)	922 (70.9)	0.41
Statins	11 (32.4)	51 (75.0)	< 0.001	522 (48.5)	1015 (78.0)	< 0.001
ACE inhibitors	8 (23.5)	22 (32.4)	0.36	431 (40.1)	652 (50.1)	< 0.001
Length of stay (days)	10 (7—14)	7 (5—13)	0.41	10 (8—14)	8 (6—12)	< 0.001

Data are number (%) or median (25th—75th percentiles). ACE: angiotensin-converting enzyme.
The length of stay was censored at the time of death for patients who died in the hospital.

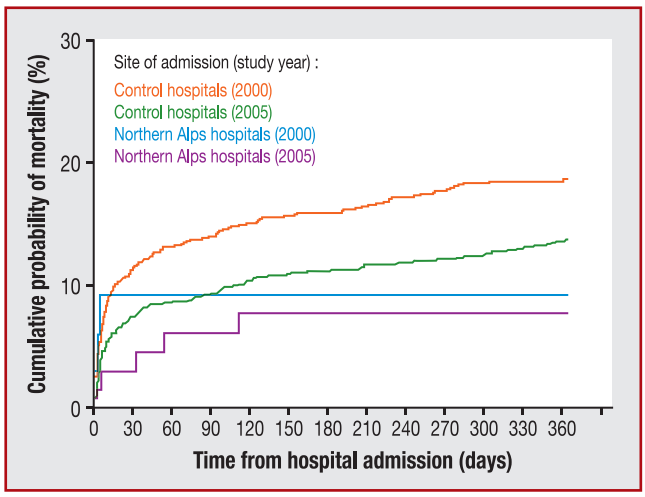

Figure 2. Comparison of cumulative mortality stratified by study group ($P = 0.002$).

Alps and control hospitals, respectively; P for interaction = 0.92).

Discussion

Consistent with previous reports, this pooled analysis of two nationwide prospective cohort studies shows substantial progress in reperfusion rates for STEMI patients between 2000 and 2005 in France. This study also indicates that the implementation of a regional system of care was followed by more frequent use of prehospital fibrinolysis and rescue or routine early coronary angiography or intervention after fibrinolysis, relative to control hospitals.

The management of acute myocardial infarction and emergency medical systems evolved between 2000 and 2005, and the increasing use of prehospital thrombolysis might have been observed without any regional initiative in the Northern Alps. However, our findings were adjusted for secular trends and sudden changes, using a controlled pre- and postintervention study design.

Despite similar admission rates by mobile emergency care units, the largest difference in change between the two study groups involved prehospital fibrinolysis (28 percentage points). This observation likely reflects compliance with our regional policy that advocates rapid administration of fibrinolysis for patients with prohibitive anticipated delays in primary PCI. The more frequent use of fibrinolysis in the prehospital setting also partly explains the concomitant decline in time from symptom onset to fibrinolysis.

Importantly, a difference in change of similar magnitude to that observed for the use of prehospital fibrinolysis was found in the percentages of patients undergoing rescue or routine early coronary angiography or intervention after fibrinolysis (20 percentage points). This result may be attributed to the opening of a new PCI centre without onsite coronary artery bypass graft capability in 2002 in the Northern Alps. It also reflects a referral practice supported by the findings from the CAPTIM trial, which failed to evidence any long-term survival advantage for primary PCI relative to a strategy of prehospital fibrinolysis followed by admission to a PCI hospital [29]. Overall, the FAST-MI study showed that patients receiving a pharmacoinvasive strategy that combined fibrinolysis with a liberal use of PCI had a similar 1-year mortality rate to patients undergoing primary PCI [21]. This finding has been confirmed by randomized trials that demonstrated the benefit of routine early transfer for PCI after fibrinolysis [30].

In contrast, the use of primary PCI improved in control hospitals only, although no significant difference in change was found between the two study groups. Meanwhile, the time to primary PCI dramatically increased, reflecting the difficulties achieving timely primary PCI, especially for patients first admitted to hospitals without PCI capability. This observation is consistent with the so-called reperfusion paradox, in which efforts to increase access to primary PCI for all STEMI patients leads to unnecessary avoidance of timely fibrinolysis and delays in reperfusion therapy [31].

Despite a substantial difference in 1-year mortality at baseline (8.8% vs 16.8%), the two study groups yielded a comparable decline in adjusted hazard ratios for death (0.77 and 0.70) in 2005. Although we cannot exclude that our analysis was underpowered to detect small but clinically significant differences in mortality, this finding may be explained by the similar increases in the percentage of patients receiving reperfusion therapy, either mechanical or pharmacological, across the two study groups (11.8 and 8.0 percentage points). As noted by others [1], the timely use of some reperfusion therapy may be more important than the reperfusion therapy option. Consistently, a recent study reported substantial reductions in mortality rates following the initiation of the Reperfusion of Acute Myocardial Infarction in North Carolina Emergency Departments (RACE) programme, but these changes mirrored those observed in statewide control hospitals and those observed nationally [32].

Although we cannot determine which component of our regional system of care for STEMI patients was most effective in improving processes of care, several aspects distinguish our initiative from previous research [13,15,17,18]. First, our system of care has been implemented through an integrated network encompassing all hospital-based structures in charge of patients with STEMI (i.e. emergency medical service call centres, mobile emergency care units, emergency departments, intensive care units and catheterization laboratories), regardless of their affiliation. Interhospital transfer protocols have been approved by representatives of each participating hospital; this is in accordance with a previous modelling study showing that a strategy of transporting every patient to an existing PCI centre is less costly and more effective than various hospital expansion options [33]. To avoid the diversion of patients from local community hospitals without PCI capability, patients directed to PCI centres are transferred to their local hospitals soon after their procedure.

Second, unlike other systems for reperfusion that rely on local ambulances [1], both prehospital transportation and interhospital transfer of STEMI patients are operated by mobile emergency care units staffed by emergency or critical care physicians [25]. This allows early recognition of STEMI, substantial reduction in delays in reperfusion therapy and management of life-threatening complications, such as arrhythmias, during transportation [34]. Despite long

distances or driving times, our system of care relied predominantly on ground medical transport, although other systems advocate helicopter transfer when the anticipated transport time is longer than 40 minutes [13]. However, some general practitioners in ski resorts or sparsely populated areas may administer prehospital fibrinolysis to provide timely access to reperfusion therapy, as part of our regional initiative [35].

Third, the regional healthcare authority played a leading role in encouraging the development of our integrated network. Financial incentives and contract arrangements were set up to encourage collaboration between PCI and non-PCI hospitals. A dedicated team is funded to ensure the coordination and maintenance of the regional system of care. The impact of regionalization on access to timely reperfusion is monitored continuously.

Study limitations

Some study limitations deserve mention. First, this study was not randomized in design and therefore the results may be confounded by differences in casemix as well as secular trend or sudden changes in processes of care. Yet, unlike previous reports, our study included a control group consisting of 153 hospitals in order to account for evolving therapies and other temporal factors. Moreover, this observational study addresses an important question that is unlikely to be studied by randomized controlled trials because the implementation of systems of care for STEMI depends on many factors, including legislation and local policies, available resources, purchaser and payer interests and population preferences.

Second, the limited sample size implied that estimates were imprecise and potentially unreliable for processes of care and outcomes among patients enrolled in Northern Alps hospitals. Although the findings support our study hypothesis, they should be regarded with caution.

Third, to the best of our knowledge, no concurrent initiative involving control hospitals was implemented between 2000 and 2005, although this possibility cannot be formally ruled out. However, such concurrent initiatives would contribute to attenuating the differences in processes of care and patient outcomes observed between Northern Alps and control hospitals.

Fourth, seven of 15 (47%) Northern Alps hospitals and 153 of 359 (43%) control hospitals participated, on a voluntary basis, in the USIC 2000 and FAST-MI studies. Hence, they may not be representative of the hospitals with intensive care units that treated patients with acute myocardial infarction in France. Additionally, these findings may not extend to patients treated in other geographical locations because processes of care for patients with acute myocardial infarction have been shown to vary across countries.

Fifth, our study was based on data collected in 2000 and 2005 and may not reflect current practices. Our regional policy has evolved, promoting a more frequent use of primary PCI for patients, with timely access to PCI centres in order to comply with published evidence. Unfortunately, more recent data were not available to address this issue at the time the present analysis was performed.

Conclusion

In conclusion, regionalization of care in a predominantly mountainous area improved access to timely reperfusion therapy through the more frequent use of prehospital fibrinolysis and rescue or routine early PCI after fibrinolysis. These findings provide additional support for implementing regional systems of care for STEMI, although their impact on clinical outcomes deserves further study.

Disclosure of interest

N.D. has received research grants from AstraZeneca, Eli-Lilly, Merck, Pfizer, Sanofi-Aventis, Servier and The Medicines Company; he has also received fees for speaking at industry-sponsored symposia and/or consulting for AstraZeneca, Bristol-Myers Squibb, Boehringer-Ingelheim, GlaxoSmithKline, Lilly, Menarini, MSD-Schering, Novartis, Novo, Pfizer, Sanofi-Aventis, Servier and The Medicines Company. The other authors declare that they have no conflicts of interest concerning this article.

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